The invention claimed is:

1. A method for analyzing the structural properties of an RNA molecule comprising:

(a) contacting said RNA molecule with a cleavage reagent capable of partially hydrolyzing said RNA molecule, wherein said partial hydrolysis is attenuated in a region of said RNA molecule that is relatively inaccessible to solvent; and

(b) separating and detecting the cleaved RNA by IP-RP-HPLC, wherein the absence of cleavage events in a region of the RNA indicates that said region is relatively inaccessible to solvent.

2. The method of Claim 1, wherein said IP-RP-HPLC employs a separation medium that is substantially free of multivalent cations that are capable of interfering with polynucleotide separations.

3. The method of Claim 2, wherein said separation medium comprises particles selected from the group consisting of silica, silica carbide, silica nitrite, titanium oxide, aluminum oxide, zirconium oxide, carbon, insoluble polysaccharide, and diatomaceous earth, the particles having separation surfaces which are coated with a hydrocarbon or non-polar hydrocarbon substituted polymer, or have substantially all polar groups reacted with a non-polar hydrocarbon or substituted hydrocarbon group, wherein said surfaces are non-polar.

4. The method of Claim 2, wherein said separation medium comprises polymer beads having an average diameter of 0.5 to 100 microns, said beads being unsubstituted polymer beads or polymer beads substituted with a moiety selected from the group consisting of hydrocarbon having from one to 1,000,000 carbons.

5. The method of Claim 4, wherein said beads are substituted with a moiety selected from the group consisting of methyl, ethyl, or hydrocarbon having from 23 to 1,000,000 carbons.

6. The method of Claim 2, wherein said separation medium comprises a monolith.

7. The method of Claim 2, wherein said separation medium has been subjected to acid wash treatment to remove any residual surface metal contaminants.

8. The method of Claim 2, wherein said separation medium has been subjected to treatment with a multivalent cation binding agent.

9. The method of Claim 2, wherein said IP-RP-HPLC employs a mobile phase comprising a solvent selected from the group consisting of alcohol, nitrile, dimethylformamide, tetrahydrofuran, ester, ether, and mixtures of one or more thereof.

10. The method of Claim 9, wherein said mobile phase comprises acetonitrile.

11. The method of Claim 2, wherein said mobile phase comprises a counterion agent selected from the group consisting of lower alkyl primary amine, lower alkyl secondary amine, lower alkyl tertiary amine, lower trialkylammonium salt, quaternary ammonium salt, and mixtures of one or more thereof.

12. The method of Claim 11, wherein said counterion agent is selected from the group consisting of octylammonium acetate, octadimethylammonium acetate, decylammonium acetate, octadecylammonium acetate, pyridiniumammonium acetate, cyclohexylammonium acetate, diethylammonium acetate, propylethylammonium acetate, propyldiethylammonium acetate, butylethylammonium acetate, methylhexylammonium acetate, tetramethylammonium acetate, tetraethylammonium acetate, tetrapropylammonium acetate, tetrabutylammonium acetate, dimethydiethylammonium acetate, triethylammonium acetate, tripropylammonium acetate, tributylammonium acetate, tetrapropylammonium acetate, tetrabutylammonium acetate, triethylammonium hexafluoroisopropyl alcohol, and mixtures of one or more thereof.

13. The method of Claim 12, wherein said counterion agent is tetrabutylammonium acetate.

14. The method of Claim 12, wherein said counterion agent is triethylammonium acetate.

15. The method of Claim 11, wherein said counterion agent includes an anion selected from the group consisting of acetate, carbonate, phosphate, sulfate, nitrate, propionate, formate, chloride, and bromide.

16. The method of Claim 2, wherein said detection is achieved using Matched Ion Polynucleotide Chromatography.

17. The method of Claim 2, wherein said RNA molecule is detectably labeled.

18. The method of Claim 17, wherein said detectable label is fluorescent.

19. The method of Claim 118, wherein said detectable label is selected from the group consisting of FAM, JOE, TAMRA, ROX, HEX, TET, Cy3, and Cy5.

20. The method of Claim 19, wherein said detectable label is FAM.

21. The method of Claim 2, wherein said cleavage reagent is a hydroxyl radical.

22. The method of Claim 21, wherein said hydroxyl radical is generated using $Fe(EDTA)^{2-}$.

23. The method of Claim 2, wherein said cleavage reagent is a nuclease.

24. The method of Claim 23, wherein said nuclease is an RNase.

25. The method of Claim 2, wherein said IP-RP-HPLC separation is phased by running a parallel RNA cleavage reaction.

26. The method of Claim 25, wherein said DNA cleavage reaction is an RNA sequencing reaction.

27. The method of Claim 2, wherein said RNA molecule includes region that is relatively inaccessible to solvent owing to intramolecular interactions.

28. The method of Claim 2, wherein said method is used to characterize the three-dimensional structure of said RNA molecule.

29. The method of Claim 2, wherein said RNA molecule includes region that is relatively inaccessible to solvent owing to intermolecular interactions.

30. The method of Claim 2, wherein said RNA molecule is a ribozyme, and wherein said method is used to characterize the interaction of said ribozyme with a substrate.

31. The method of Claim 29, wherein said intermolecular interaction is between said RNA molecule and an RNA-binding protein.